IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Bendele et al.

Serial No.: Not Yet Received

Group Art Unit No.: 1646

Filed: July 17, 2001

Examiner: E. O'Hara

For: COMBINATION THERAPY USING A TNF BINDING PROTEIN FOR TREATING TNF-MEDIATED DISEASES

Docket No.: A-430F

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend the referenced application as follows:

In the Specification

At page 1, line 3, insert the following paragraph:

This application is a divisional of application Serial No. 09/326,394 filed June 4, 1999, which is a continuation of PCT/US97/22733, filed December 8, 1997, which claims benefit to U.S. Provisional Serial No. 60/032,587, filed December 6, 1996, U.S. Provisional Serial No. 60/036,355, filed January 23, 1997, U.S. Provisional Serial No. 60/039,315, filed February 7, 1997 and U.S. Provisional Serial No. 60/052,023, filed July 9, 1997, all of which are hereby incorporated by reference.

In the Claims

Please cancel claims 2-26 and insert the following new claims:

27. The method of treatment of an acute or chronic inflammatory disease of Claim 1, which comprises administering a TNF binding protein in combination with the prior, concurrent, or post-administration of a COX2 inhibitor.

28. The method of treatment according to claim 27, wherein the COX2 inhibitor is celecoxib.

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Lynne Buchsbaum
Printed Name

Lynne Buchsbaum
Signature

29. The method of treatment according to claim 27, wherein the acute or chronic inflammatory disease is a TNF-mediated disease.

30. The method of treatment according to claim 27, wherein said TNF binding protein comprises a sequence which is at least about 80% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

31. The method of treatment according to claim 27, wherein said TNF binding protein comprises a sequence which is at least about 90% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

32. The method of treatment according to claim 27, wherein said TNF binding protein comprises a sequence which is at least about 95% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

33. The method of treatment according to claim 27, wherein said TNF binding protein comprises a sequence which is at least about 99% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

34. The method of treatment according to claim 27, wherein said TNF binding protein comprises an amino acid having a sequence of SEQ ID NO: 2.

35. The method of treatment according to claim 27, wherein said TNF binding protein comprises a deletion variant of SEQ ID NO: 2 having an N-terminal or C-terminal deletion.

36. The method of treatment according to claim 27, wherein said TNF binding protein is non-glycosylated.

37. The method of treatment according to claim 27, wherein said TNF binding protein is glycosylated.

38. The method of treatment according to claim 30, wherein an additional amino acid is added to the sequence of SEQ ID NO: 2 and the additional amino acid is an N-terminal methionine having the residue number "0".

39. The method of treatment according to claim 27, wherein said TNF binding protein is produced by recombinant DNA methods.

40. The method of treatment according to claim 27, wherein said inflammatory disease is an inflammatory disease of a joint.

41. The method of treatment according to claim 27, wherein said inflammatory disease is rheumatoid arthritis.

42. A dosage unit, comprising a COX2 inhibitor for the treatment of an acute or chronic inflammatory disease in a patient and a TNF binding protein, wherein said dosage unit allows for administration of the COX2 inhibitor prior, concurrent, or after administration of the TNF binding protein.

43. The dosage unit according to claim 42, wherein the COX2 inhibitor is celecoxib.

44. The dosage unit according to claim 42, wherein the acute or chronic inflammatory disease is a TNF-mediated disease.

45. The dosage unit according to claim 42, wherein said TNF binding protein comprises a sequence which is at least about 80% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

46. The dosage unit according to claim 42, wherein said TNF binding protein comprises a sequence which is at least about 90% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

47. The dosage unit according to claim 42, wherein said TNF binding protein comprises a sequence which is at least about 95% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

48. The dosage unit according to claim 42, wherein said TNF binding protein comprises a sequence which is at least about 99% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

49. The dosage unit according to claim 42, wherein said TNF binding protein comprises an amino acid having a sequence of SEQ ID NO: 2.

50. The dosage unit according to claim 42, wherein said TNF binding protein comprises a deletion variant of SEQ ID NO: 2 having an N-terminal or C-terminal deletion.

51. The dosage unit according to claim 42, wherein said TNF binding protein is non-glycosylated.

52. The dosage unit according to claim 42, wherein said TNF binding protein is glycosylated.

53. The dosage unit according to claim 45, wherein an additional amino acid is added to the sequence of SEQ ID NO: 2 and the additional amino acid is an N-terminal methionine having the residue number "0".

54. The dosage unit according to claim 42, wherein said TNF binding protein is produced by recombinant DNA methods.

55. The dosage unit according to claim 42, wherein said inflammatory disease is an inflammatory disease of a joint.

56. The dosage unit according to claim 42, wherein said inflammatory disease is rheumatoid arthritis.

57. A pharmaceutical composition, comprising a TNF binding protein and a COX2 inhibitor for the treatment of an acute or chronic inflammatory disease in a patient .

58. The pharmaceutical composition according to claim 57 wherein the COX2 inhibitor is celecoxib.

59. The pharmaceutical composition according to claim 57, wherein the acute or chronic inflammatory disease is a TNF-mediated disease.

60. The pharmaceutical composition according to claim 57, wherein said TNF binding protein comprises a sequence which is at least about 80% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

61. The pharmaceutical composition according to claim 57, wherein said TNF binding protein comprises a sequence which is at least about 90% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

62. The pharmaceutical composition according to claim 57, wherein said TNF binding protein comprises a sequence which is at least about 95% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

63. The pharmaceutical composition according to claim 57, wherein said TNF binding protein comprises a sequence which is at least about 99% homologous to the amino acid sequence of SEQ ID NO: 2 or to the amino acid sequence of SEQ ID NO: 4.

64. The pharmaceutical composition according to claim 57, wherein said TNF binding protein comprises an amino acid having a sequence of SEQ ID NO: 2.

65. The pharmaceutical composition according to claim 57, wherein said TNF binding protein comprises an N-terminal or C-terminal deletion of SEQ ID NO: 2.

66. The pharmaceutical composition according to claim 57, wherein said TNF binding protein is non-glycosylated.

67. The pharmaceutical composition according to claim 57, wherein said TNF binding protein is glycosylated.

68. The pharmaceutical composition according to claim 60, wherein an additional amino acid is added to the sequence of SEQ ID NO: 2 and the additional amino acid is an N-terminal methionine having the residue number "0".

69. The pharmaceutical composition according to claim 57, wherein said TNF binding protein is produced by recombinant DNA methods.

70 The pharmaceutical composition according to claim 57, wherein said inflammatory disease is an inflammatory disease of a joint.

71. The pharmaceutical composition to claim 57, wherein said inflammatory disease is rheumatoid arthritis.

The applicant requests submission of these amendments. The Commissioner is hereby authorized to charge any fees which may be required or credit any overpayment to Deposit Account No. 01-0519 in the name of Amgen Inc.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

This application is a division of application Serial No. 09/326,394 filed June 4, 1999, which is a continuation of PCT/US97/22733, filed December 8, 1997, which claims benefit to U.S. Provisional Serial No. 60/032,587, filed December 6, 1996, U.S. Provisional Serial No. 60/03,355, filed January 23, 1997, U.S. Provisional Serial No. 60/039,315, filed February 7, 1997 and U.S. Provisional Serial No. 60/052,023, filed July 9, 1997, all of which are hereby incorporated by reference.